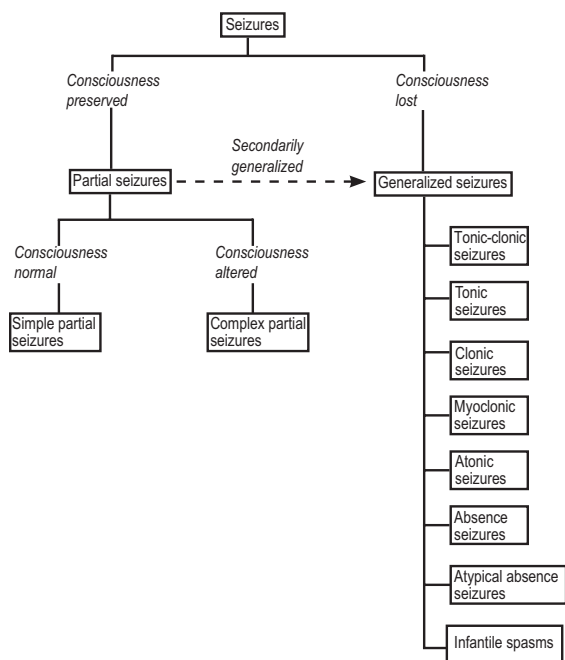


Seizures

Jennifer M. Naticchia and David M. Bercaw

Few clinical events present as dramatically as the patient with a generalized tonic-clonic seizure, nor as subtly as the patient with an *absence* seizure. The clinician's goal is to accurately and effectively diagnose and treat such patients. Clinicians should differentiate between epileptic seizures (therefore likely recurrent)—and secondary seizures (therefore possibly curable). This aids in the decision as to whether to initiate antiepileptic drug therapy. Secondary causes of seizure include infection, cerebrovascular accident, tumor, congenital injury or malformation, AVM, and others. In considering the diagnosis of seizure, the clinician must take into account the medical, social, and psychologic implications of labeling a patient as “epileptic.”



This chapter outlines the common clinical manifestations of seizures classified into three main categories: partial, generalized, and unclassified epileptic seizures. Partial seizures begin as a focal transient alteration of function compared with generalized seizures, which start with loss of consciousness and involve both sides of the body. Unclassified epileptic seizures usually have nondistinctive features presenting in neonates and infants.

ABSENCE SEIZURES

Absence seizures are a type of generalized seizure formerly known as petit mal seizures. They mainly occur in children and may occur daily, often with many episodes in a 24-hour period. These types of seizures resemble a staring spell that may be unrecognized until a teacher notes poor school performance. No postictal phase is present with these episodes. Atypical absence seizures are associated with myoclonic activity of the facial muscles or extremities. Absence seizures are associated with childhood absence epilepsy. Children with absence seizures may later develop tonic-clonic seizures and their condition is then classified as juvenile absence epilepsy.

Signs

- “Staring spell” that lasts from 4 to 20 seconds +++++
- Child resumes preseizure activity ++++
- May be associated with rolling of the eyes or flutter of eyelids
- Unresponsiveness ++++
- Partial awareness +++

Workup

- Normal lab analysis
- Normal radiologic evaluation
- EEG
- Seizure is induced with hyperventilation and characteristic spike and wave formations are noted at 1.5 to 4 Hz/sec.
- The EEG spikes are irregular in atypical absence seizures with postictal slowing.

Comments and Treatment Considerations

Ethosuximide and valproate are more commonly used for treatment. Valproate is the drug of choice if patients have tonic-clonic episodes or myoclonic jerks. Other possible therapies include lamotrigine, zonisamide, benzodiazepines, acetazolamide, levetiracetam, topiramate, and ketogenic diet.

Approximately 70% of children outgrow absence seizures, especially if the seizures start before age 10. Some may go on to develop juvenile absence epilepsy or juvenile myoclonic epilepsy. Unfavorable prognosis is associated with generalized tonic-clonic activity in the active stage of absence, myoclonic jerks, eyelid or perioral myoclonia, and atypical EEG features.

FEBRILE SEIZURES

The most common type of convulsive disorder in children younger than 5 years of age is a simple febrile seizure. Febrile seizures occur during a febrile illness and in the absence of a CNS infection, acute electrolyte imbalance, or known seizure disorder. They tend to occur within the first 24 hours of a febrile illness, and with temperatures averaging 39.8° C. The age groups most commonly experiencing febrile seizures are patients ages 6 months to 5 years, with peak occurrence in children 18 to 24 months old. Approximately 3% to 5% of children will experience a febrile seizure before age 5. A simple febrile seizure is described as a generalized seizure lasting less than 15 minutes and does not recur in 24 hours. A complex febrile seizure can have focal features, last more than fifteen minutes, and may recur within a 24-hour period. Simple febrile seizures comprise 80% of febrile seizures, carry few risks of complications, and have excellent short- and long-term prognoses. Most children who experience a simple febrile seizure do not require hospitalization. Parents should be educated and reassured about the benign nature of febrile seizures.

Symptoms

- History of fever
- Drowsiness following seizure activity

Signs

- Generalized tonic-clonic activity lasting less than 15 minutes
+++++
- Rectal temperature greater than 38° C +++++
- Brief postictal phase +++++

Workup

- Thorough history and physical examination
- Laboratory tests as indicated, typically only if history or physical examination suggestive of another process (e.g., dehydration)
- If seizure occurs after the second day of febrile illness, lumbar puncture should be considered.
- If less than 1 year old, consider lumbar puncture because meningeal signs may be absent.
- CT, MRI, EEG: not indicated in simple febrile seizure with normal neurologic examination

Comments and Treatment Considerations

Treat the cause of the fever (most fevers are due to viral illness). Reduce fever with antipyretics. Anticonvulsants are not indicated in a seizure lasting less than 5 minutes. If a seizure lasts more than 5 minutes, benzodiazepines are first-line therapy.

Approximately one third of children with febrile seizures will experience a recurrence of seizure activity. In children who have their first febrile seizure before 18 months of age and a positive family history of febrile seizures in a first-degree relative, the risk

of recurrence is increased. Risk of recurrence declines to zero by 5 years of age. The risk of developing epilepsy in a child with a history of febrile seizure is 1% higher than the general population. Patients with febrile seizures are not at higher risk for developing more serious bacterial illnesses. Most important, long-term consequences are rare in children who are otherwise healthy.

PARTIAL SEIZURES

All seizures are caused by abnormal electrical disturbances in the brain. Partial seizures involve electrical disturbances limited to specific areas of the brain, which may cause changes in attention, movement, and behavior. Foci in the brain tissue giving rise to these disturbances may be congenitally acquired, or they may develop following head trauma, infections, stroke, or certain other conditions. In many patients, no obvious cause can be determined. Partial seizures are subdivided into simple partial seizures and complex partial seizures.



SIMPLE PARTIAL SEIZURES

These seizure types are classified as “simple” because consciousness is not impaired and “partial” because only part of the cortex is disrupted by the seizure.

Symptoms

- Motor
 - Single or multiple muscle jerks
 - Rhythmic jerking movements of the face, arm or leg on the side of the body opposite to the involved cortex (jacksonian seizure)
 - Spasms or rigidity of one unilateral body region
 - Eye deviation
 - Abnormal head movements
- Somatosensory
 - Unusual sensations affecting regular or special sensory symptoms (olfactory, visual, gustatory)
- Autonomic
 - Epigastric sensation
 - Nausea
 - Sweating
- Psychologic
 - Memory (e.g., déjà vu)
 - Emotional disturbance (e.g., fear)

Signs

- Single or multiple muscle jerks
- Rhythmic jerking movements of the face, arm, or leg on the side of the body opposite to the involved cortex (jacksonian seizure)

- Spasms or rigidity of one unilateral body region
- Eye deviation
- Abnormal head movements
- Normal consciousness and awareness
- Postictal focal neurologic deficit (hemiparesis or aphasia)



COMPLEX PARTIAL SEIZURES

These seizures are classified as “complex” because consciousness is impaired, but still “partial” because only part of the cortex is involved. This type of seizure usually lasts less than 3 minutes.

Symptoms

- May be preceded by a warning or aura (auras are simple partial seizures with symptoms as described following, most commonly somatosensory, autonomic, and psychologic)

Signs

- Altered consciousness/awareness such as unresponsiveness or staring
- Repetitive behaviors (automatisms) such as lip smacking, grimacing, swallowing, picking, manipulating objects, snapping fingers, repeating words or phrases, walking, running, or undressing
- Postictal focal neurologic deficit resolving within 48 hours
- Todd's paralysis—Transient paralysis following seizure
- Postictal phase—Somnolence, confusion, headache (up to several hours)



SECONDARILY GENERALIZED SEIZURES

Partial seizures, both simple and complex, can progress to a generalized seizure (GS). A simple partial seizure can directly evolve into a GS or, it may first evolve to a complex partial seizure, which then evolves to a GS.

Workup

- It is often difficult to diagnose a single focal seizure. A diagnosis is easier to make in patients who have recurrent, stereotyped seizures.
- Thorough history and physical examination
- Differentiate transient, provoked seizure (with an underlying cause) from epilepsy.
- Blood tests: serum glucose and electrolytes (sodium, calcium, magnesium); renal function tests; hepatic function tests if liver impairment is suspected; CBC if infection is suspected; and urine screen for drugs if abuse is suspected
- Lumbar puncture with signs that suggest CNS infection, for example, altered mental status, fever, or nuchal rigidity

- Classify type of seizure based on signs and symptoms
- EEG can show characteristic changes confirming partial (focal) seizures, and may show the focus. A normal EEG does not rule out seizures. Sensitivity is 50%; specificity is 98% to 99%.
- Neuroimaging: imaging must be performed in all patients with partial-onset seizures to identify any structural brain disease as an underlying cause and exclude an expanding mass lesion that might require acute intervention. MRI is the preferred imaging option.

Comments and Treatment Considerations

Administer first-aid measures as appropriate: protect the person from injury during the seizure and protect the airway. Treat identified underlying causes: discontinue medication and manage tumors or other brain lesions. Prescribe antiepileptic drugs (AEDs) in patients with recurrent seizures. Partial complex seizures are treated with the same AEDs used for generalized seizures (with the exception of ethosuximide used to treat absence seizure).

Follow-up includes review of the need for drugs and monitoring for side effects.

Surgery performed for refractory seizures include vagal nerve stimulator or removal of the abnormal brain cells/tissue causing seizures.

Identify and avoid and eliminate known precipitants. Studies suggest more than 60% of reported seizures are associated with certain precipitants (e.g., stress and sleep deprivation).

TONIC-CLONIC SEIZURES (GRAND MAL SEIZURES)

The seizure begins with a sudden loss of consciousness associated with a tonic phase characterized by generalized muscular stiffening of the trunk and extremities. Muscle movement or eye deviation that begins or is exhibited primarily on one side should raise the suspicion that the seizure is not truly generalized, but is focal in origin—leading to a more intense search for underlying CNS pathology. The tonic phase merges into the clonic phase, consisting of rhythmic, symmetric, and synchronous muscular jerking movements. Rarely, a generalized seizure may exhibit only a tonic phase (tonic seizure) or a clonic phase (clonic seizure), but in these cases the evaluation should be the same as for a generalized tonic-clonic event. It is followed by the recovery phase, during which there is a gradual return to consciousness that usually occurs within 40 seconds to 3 minutes from seizure onset. Finally, the seizure ends with a postictal phase characterized by confusion, stupor, sleepiness, and headache. The postictal phase may last from minutes to hours.

Symptoms

- Usually no prodromal symptoms or aura (otherwise, consider primary focal seizure that then generalizes)
- Postictal state
- Amnesic for the event

Signs

- Sudden loss of consciousness +++++
- Expiratory “scream” ++++
- Drooling, pupillary dilation, stertorous respirations
- Urinary or fecal incontinence +++
- Tachycardia and elevated blood pressure
- No focal neurologic deficits

Workup

- Inquire about withdrawal from alcohol, benzodiazepines, barbiturates
- Serum glucose and sodium
- Consider serum calcium, magnesium, complete blood count, liver function tests
- Consider toxicology screen
- Pregnancy test on women of childbearing age (may affect choice of AEDs)
- Serum drug levels (if already on AEDs)
- CT head as soon as possible if:
 - Acute intracranial process suspected
 - History of acute head trauma
 - History of malignancy
 - Immunocompromised patient
 - Fever
 - Persistent headache
 - New focal neurologic examination finding
 - Age more than 40 years
 - Focal onset before generalization
- Consider CT, or preferably MRI, in any patient with first-time seizure, even if patient is alert and has returned to baseline
- Consider lumbar puncture if:
 - Fever
 - Immunocompromised (especially if HIV positive)
 - History of malignancy known to metastasize to the meninges
 - Age less than 6 months
- Consider EEG
 - Most sensitive when performed within 24 hours of seizure (29% sensitivity)
 - If normal, consider sleep-deprived EEG (48% sensitivity)

Comments and Treatment Considerations

In acute patients, protect airway and tongue. Administer oxygen and IV access if prolonged seizure. Consider IV glucose and thiamine. Place in left lateral decubitus position. If seizure lasts longer than 5 minutes administer diazepam 0.1 mg/kg slow IV push; maximum 5 mg/min (maximum dose 5 mg in infants; 10 mg in children; 30 mg in adults), or lorazepam 1 to 2 mg IM or IV.

For status epilepticus (continuous seizure for more than 30 minutes or repeated motor seizure without recovery of baseline consciousness between attacks):

- Airway, breathing, and circulation (ABCs)
- Low threshold for intubation

- Monitor pulse oximetry
- Glucose
- IV access
- Watch for hypo- or hypertension
- Cardiac monitor
- Monitor temperature for hyperthermia
- Goal is control of seizure within 30 minutes
- Lorazepam 2 mg/min IV; maximum 10 mg
- Phenytoin 15 to 20 mg/kg up to 30 mg/kg IV at 25 to 50 mg/kg/min
- If patient is known to have been on phenytoin give 9 mg/kg IV until drug level is back
- Fosphenytoin can be given at 100 to 150 mg phenytoin equivalents per minute IV or IM.
- If seizure continues:
 - Phenobarbital 10 to 20 mg/kg IV at 100 mg/hr *or*
 - Valproic acid 15 to 30 mg/kg
- If seizure still continues:
 - Pentobarbital anesthesia 5 mg/kg IV at 25 mg/min, then 2.5 mg/kg/hr *or*
 - Diazepam 100 mg in 500 mL D₅W IV drip at 40 mL/hr
 - Lidocaine 100-mg IV bolus
 - Chloral hydrate 30 mg/kg PR
 - Isoflurane (general anesthesia)
 - Paralysis with pancuronium, with intubation
- Follow CK and creatinine for possible rhabdomyolysis
- Thiamine 100 mg IV and Mg⁺⁺ 1 to 2 g for alcoholic and/or malnourished patients

Admit the patient to the hospital if he or she is experiencing a prolonged postictal state or drug or alcohol withdrawal, is a febrile patient, presents with expanding mass on imaging, has experienced recent trauma, presents with focal neurologic signs or status epilepticus, or has compliance issues or inadequate supervision at home.

Further treatment does not usually require a need to start AEDs if this is the first seizure and the patient has normal neurologic examination, blood work, imaging studies, and EEG. However, there may be a need to start AEDs if this is a second seizure and there is no treatable, curable, or preventable underlying cause. Appropriate therapies include phenytoin orally or IV; fosphenytoin IV or IM; carbamazepine; valproate; and phenobarbital (more side effects).

Consider the patient's occupation and public safety. You may need to notify the state department of motor vehicles, depending on state law. Consider a Medic-Alert bracelet (800-736-3342).

The physician's role in the evaluation of generalized tonic-clonic seizure is to exclude an underlying systemic cause and to determine the likelihood of recurrence. The diagnosis of epilepsy is often difficult to establish, given the low sensitivity of EEGs. Deciding whether to initiate AED therapy is often difficult and may have profound physical, psychologic, occupational, and legal implications for the patient. A complete and accurate history, combined with careful physical examination and appropriate testing, is of paramount

importance in establishing the correct diagnosis. Further testing, including imaging studies, is required if the patient has any focal neurologic findings.

References

- Behrman R, Kliegman R, Jenson H, editors: *Nelson textbook of pediatrics*, 16th ed, Philadelphia, 2000, Saunders, pp 1817–1825.
- Betting LE, Mory SB: MRI volumetry shows increased anterior thalamic volumes in patients with absence epilepsy, *Epilepsy Behav* 8(3):575–580, 2006.
- Cameron H: Neurology. In Gunn V, Nechyba C, editors: *The Harriet Lane handbook*, 16th ed, Philadelphia, 2002, Mosby.
- Chan CH, Briellman RS: Thalamic atrophy in childhood absence epilepsy, *Epilepsia* 47(2):399–405, 2006.
- Chen DK, So YT, Fisher RS: Use of serum prolactin in diagnosing epileptic seizures: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology, *Neurology* 67(3):544–545, 2005.
- Freedman S, Powell E: Pediatric seizures and their management in the emergency department, *Clin Pediatr Emerg Med* 4:195–206, 2003.
- Grosso S, Galimberti D: Childhood absence epilepsy: evolution and prognostic factors, *Epilepsia* 46(11):1796–1801, 2005.
- Hirtz D, Ashwal S, Berg A, Bettis D, Camfield C, et al: Practice parameter: evaluating a first nonfebrile seizure in children, *Neurology* 55(5):616–623, 2000.
- King MA, Newton MR, Jackson GD, et al: Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients, *Lancet* 352(9133):1007–1011, 1998.
- Lowenstein DH: Seizures and epilepsy. In Kasper D, Braunwald E, et al: *Harrison's principles of internal medicine*, 16th ed, New York, 2005, McGraw-Hill, pp 1041–1112.
- Millar J: Evaluate and treatment of the child with febrile seizure, *Am Fam Physician* 73:1761–1766, 2006.
- Moljedic S, Krampf K: A mutation in the GABA receptor alpha (1)-subunit is associated with absence, *Epilepsy Ann Neurol* 59(6):983–987, 2006.
- Moore-Sledge CM: Evaluation and management of first seizures in adults, *Am Fam Physician* 56(4):1113–1120, 1997.
- Noebels JL, Tharp BR: Absence seizures in developing brain. In Schwartzkroin P, Cary, NC, Moshé SL, Noebels J, Swann J (editors): *Brain development in epilepsy*, 1995, Oxford University Press, p 66.
- Peloquin JB, Khosravani H, Barr W, Bladen C, et al: Functional analysis ca 3.2 T-type calcium channel mutations linked to childhood absence epilepsy, *Epilepsia* 47(3):655–658, 2006.
- Posner EB, Mohamed K: Ethosuximide, sodium valproate and lamotrigine for absence seizures in children and adolescence, *Cochrane Database Syst Rev*, 2005, CD003032.
- Posner EB: Pharmacological treatment of childhood absence epilepsy, *Exp Rev Neurother* 6(6):855–862, 2006.
- Sadlier LG, Farrell MB: Electroclinical features of absence epilepsy, *Neurology* 67(3):413–418, 2006.
- Segan S: *Absence seizures*. Available at www.emedicine.com/neuro/topic3.htm.
- Shneker BF, Fountain NB: Epilepsy, *Dis Mon* 49(7):426–478, 2003.
- Vining EP, Freeman JM: A multicenter study of the efficacy of the ketogenic diet, *Arch Neurol* 55:1433–1437, 1998.
- Warden CR, Zibuleswsky J, Mace S, et al: Evaluation and management of febrile seizures in the out-of-hospital and emergency department settings, *Ann Emerg Med* 41:215–222, 2003.
- Wilfong A, Schultz R: Zonisamide for absence seizures, *Epilepsy Res* 64(1–2):31–34, 2005.